

REMARKS

Per the Final Office Action mailed February 16, 2006 and the Advisory Action mailed May 24, 2006, Claims 1, 7, 8, 10, 36, 38 and 42 are pending in the application. Claims 1, 7, 8, 10, 36, 38 and 42 stand as rejected under 35 U.S.C. §112, first paragraph. Claims 36 and 38 stand as rejected under 35 U.S.C. §102(a). Claim 44 has been amended herein solely for clarification purposes, no new matter has been added. Claims 36, 38, 40 and 42 have been canceled herein. In view of the following amendments and remarks, reconsideration and withdrawal of the rejections are respectfully requested.

Rejections under 35 U.S.C. §112

Claims 1, 7, 8, 10, 36, 38 and 42 stand as rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner alleges that the claims are not enabled because there is insufficient guidance and objective evidence that one of ordinary skill in the art would know how to predictably use the claimed invention in any substantial manner. Specifically, the Examiner states that there is no credible enablement for any substantial or well-established utility for the claimed polynucleotides.

Claims 36, 38 and 42 have been canceled herein, and thus, the rejection is moot with respect to the claims.

Applicants strongly disagree with the Examiner's assessment of claims 1, 7, 8, and 10 based on the language utilized in the rejection. Accordingly, the rejection is more in line with 35 U.S.C. §101, and has been mischaracterized as a rejection under §112, first paragraph. For example, terms such as "substantial utility,"¹ "credible utility,"² and "specific utility"³ are indicative of a rejection under §101.⁴

The Applicants' assertion of utility creates a presumption of utility that is sufficient to satisfy the utility requirement under §101.⁵ In addition to such a presumption, "[s]pecial care ...should be taken when assessing the credibility of an asserted therapeutic utility for a claimed invention. In such cases, a previous lack of success in treating a disease or condition, or the absence of a proven animal model for testing the effectiveness of drugs for treating a disorder in

¹ See the Advisory Action mailed May 24, 2006, p. 3, l. 19; p. 4, l. 2; and p. 7, l. 12

² See the Advisory Action mailed May 24, 2006, p. 3, l. 17

³ See the Advisory Action mailed May 24, 2006, p. 4, l. 17

⁴ See MPEP Section 2164.07 ("The requirement of 35 U.S.C. [§]101 is that some specific, substantial, and credible use be set forth for the invention. On the other hand, 35 U.S.C. [§]112, first paragraph requires an indication of how the use ... can be carried out, i.e., how the invention can be used.").

humans, should not, standing alone, serve as the basis for challenging the asserted utility under 35 U.S.C. [§]101.”⁶ This is particularly applicable to the instant case, which is directed to diagnostic and therapeutic uses for BRCC-2, where it has only been offered that “[the] Examiner is not suggesting that the claimed polynucleotides are not involved in *any* raf pathway; however, Examiner is stating that the claimed polynucleotides cannot be used in any substantial manner with an expectation of success.”⁷ Such a conclusory statement is not the appropriate basis upon which to base the rejection, and therefore, the rejection should be withdrawn.

In any event, Applicants have a credible and substantial utility for the invention as claimed in claims 1, 7, 8, and 10. Moreover, as set forth below, there is a reasonable correlation between the polynucleotide activity indicated by Applicants and the proffered therapeutic use.

The BRCC-2 gene is a modulator of apoptosis. See Applicants’ specification para. [0029]. Figure 5 of the Applicants’ specification evidences that the expression of the BRCC-2 gene is decreased in human breast cancer cells treated with an antisense raf oligonucleotide (AN-raf_ODN). See Applicants’ specification para. [0030]. The AN-raf_ODN causes programmed cell death in cancer cells by decreasing the amount of proliferation and survival-promoting protein raf-1. See Applicants’ specification para. [0030]. Thus, the role of BRCC-2 was examined by examining the changes in gene expression profiles in breast cancer cells treated with antisense *raf* oligodeoxyribonucleotide (ODN). See Applicants’ specification para. [0033]. Applicants’ specification clearly states:

(Fig. 5) Treatment of MDA-MB 231 breast cancer cells with antisense *raf* ODN (ISIS 5132, 2 μ M, 48h) in the presence of lipofection led to significant inhibition of Raf-1 protein (62%) as compared to control lipofection-treated or untreated cells. Raf-1 inhibition was associated with apoptosis as indicated by a 8-fold increase in a caspase-3 like protease activity. PARP cleavage, and a 5-fold increase in the sub-G1 population was observed in antisense *raf* ODN-treated cells. [T]he differential display of mRNA strategy [was used] to identify changes in gene expression as a result of antisense raf ODN-treatment of MDA-MB 231 cells. The partial cDNA fragment of novel gene, BRCC2 (862 bp) was subcloned. Northern blot analysis revealed BRCC2 transcripts of 1.2 kb, in normal human tissues and

⁵ See MPEP Section 2107.02

⁶ See MPEP 2107.02

⁷ See the Advisory Action mailed May 24, 2006, p. 6, l. 16-19

cancer cell lines. The BRCC2 cDNA sequence revealed a putative ORF of 108 amino acids. Antisense raf ODN treatment of MDA-MB 231 cells caused inhibition of the steady state mRNA levels of BRCC2 by 42.2%.

See Applicants' specification para. [0032]. Based on these results, it was identified that BRCC-2 modulates apoptosis and thereby has a therapeutic/pharmacological utility.⁸

Also as shown by the above-identified relevant data, Applicants have established a reasonable correlation between BRCC-2's activity and its therapeutic effect. Applicants do not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor do Applicants have to provide actual evidence of success in treating humans where such a utility is asserted.⁹ Thus, Applicants have fulfilled their obligation with respect to the utility of the subject matter of claims 1, 7, 8, and 10. Therefore, Applicants respectfully request that the rejection be reconsidered and withdrawn.

In addition to Applicants satisfying the requirements under 35 U.S.C. §101, Applicants have also enabled one skilled in the art to make and use the invention as set forth in claims 1, 7, 8 and 10. For example, Applicants' specification teaches, and one skilled in the art would recognize and understand, the methods utilized to isolate the nucleic acid molecule comprising the polynucleotide encoding the amino acid sequence of SEQ ID NO: 2 as well as the polynucleotide complement of SEQ ID NO: 2. See Applicants' specification para. [0064]. The BRCC-2 gene and/or its complement sequence can serve as a probe that forms a hybrid structure with a particular target sequence (see Applicants' specification para. [0099] to [0101]) as well as a target for identifying compounds that promote apoptosis of cancer cells, particularly with respect to breast and lung cancer. See Applicants' specification para. [0033]. One skilled in the art, based on the teachings found in the specification and that which is known in the art, would readily understand, *inter alia*, how to make and use recombinant vectors comprising these sequences as well as recombinant host cells comprising the recombinant vectors. See Applicants' specification para. [0066] to [0072].

⁸ See, MPEP 2707.01 (Courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an immediate benefit to the public and thus satisfies the utility requirement); (Courts have found utility for therapeutic inventions despite the fact that an applicant is at the very early stages of development in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition.).

⁹ See, MPEP 2707.02

Rejections under under 35 U.S.C. §102(a)

Claims 36 and 38 stand as rejected under 35 U.S.C. §102(a) as being anticipated by Birren et al. (Homo sapiens chromosome 11 clones RP11-85D24 map 11, 4/22/00).

A claim is anticipated only if each and every element as set forth in the claim is described in a single prior art reference. As previously noted, Birren et al. fail to teach a polynucleotide sequence that encodes a polypeptide sequence that is 100% identical of SEQ ID NO: 2, as acknowledged by the Examiner.¹⁰ The polynucleotide complement of SEQ ID NO: 2 is an identical, reversed copy of SEQ ID NO: 2, which is just as novel. While the Examiner alleges that "...one of skill in the art anticipates a complementary polynucleotide sequence to be one which encodes a polypeptide sequence >99% identical to instant SEQ ID NO: 2,"¹¹ no objective evidence has been provided. As a result, Birren et al. fail to teach each and every element of claims 36 and 38, and therefore cannot anticipate claims 36 and 38.

However, in the interests of furthering prosecution and without acquiescing to the allegations presented in the final Office Action and/or the Advisory Action, Applicants have canceled claims 36, 38 and 42. Thus, Applicants respectfully request that the rejection be reconsidered and withdrawn.

For the reasons set forth above, the Applicant respectfully requests that all of the rejections set forth in the Office Action be reconsidered and withdrawn. It is respectfully submitted that the application is now in condition for allowance, which action is earnestly solicited. If the Examiner believes that minor amendments or correction as to matters of form will expedite allowance, the Examiner is invited to telephone the Applicant's undersigned representative.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Paul Carango", written in a cursive style.

Paul Carango
Reg. No. 42,386

TRM/PC/vbm
(215) 656-3320

¹⁰ See the Advisory Action mailed May 24, 2006, p. 7, l. 20 through p. 8, l. 1, stating that "...Birren et al teaches a polynucleotide sequence which encodes a polypeptide sequence >99% identical to instant SEQ ID NO: 2."

¹¹ See the Advisory Action mailed May 24, 2006, p. 7, l. 20 through p. 8, l. 1